Attorney Docket No.: 0925.009/11862US09

IN THE UNITED STATES
PATENT AND TRADEMARK OFFICE

In the Application of:
deBoer, *et al.*

U.S. Serial No.:

Filed: September 18, 2001

For: "Method for Treating An IgE-Mediated Disease In A Patient Using Anti-CD40 Monoclonal Antibodies" (As Amended)

Group Art Unit:

Examiner:

CERTIFICATION UNDER 37 CFR § 1.10

I hereby certify that this Continuing Application Transmittal Under 37 CFR § 1.53(b) and the documents referred to as enclosed therewith are being deposited with the United States Postal Service on September 18, 2001, in an envelope addressed to: Box Patent Application, Assistant Commissioner for Patents, Washington, D.C. 202331 utilizing the "Express Mail Post Office to Addressee" service of the United States Postal Service Under Mailing Label No. EL 849006685 US.

J. Blackburn
Jimmie Blackburn

PRELIMINARY AMENDMENT

Box Patent Application
Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

The Applicants respectfully request that the Examiner make the following amendments to the specification and the claims before considering the prosecution on the merits.

In the Title:

Please delete the title and substitute therefore:

--Method For Treating An IgE-Mediated Disease In A Patient Using Anti-CD40 Monoclonal Antibodies--.

In the Figures:

Please replace Figs. 1A, 1B and 2, with substitute Figs. 1A, 1B and 2, respectively, as attached hereto. A copy of each of Figs. 1A, 1B and 2, showing the proposed changes in red is also attached hereto.

In the Specification:

At page 1, delete lines 4-7.

Please insert at the end of the specification the three pages of the SEQUENCE LISTING, as attached to the Combined Statement that is cofiled herewith.

In the Claims:

Please delete claims 1-5, 7, 12-28 in the specification as filed.

Please add claims 29 and 30.

A copy of substitute claim 6, and all pending claims (*i.e.*, claims 6, 8-11 and 29-30) is shown on Exhibit A. A marked up copy of original claim 6, showing the changes made to arrive at substitute claim 6, is attached hereto as Exhibit B.

REMARKS

The amendments to the specification do not add new matter. In particular, the amendment to the specification at page 1, lines 5-6 merely conforms the specification to the current rule wherein the claim of priority need not be cited on the first page.

The amendments to the Figures also do not add new matter. In particular, the Applicants submit substitute Figures 1A, 1B and 2, which are already attached to the specification. A copy of original Figures 1A, 1B and 2, containing the changes shown in red, are attached hereto as Exhibit C. Specifically, substitute Figures 1A and 2 now contain the SEQ ID NOs of the nucleotide sequences disclosed therein. Substitute Figure

1B contains the corrected term "Sf9" which was incorrectly typed as "sf-9" at two locations. Support for correction of this typographical error is found throughout the specification, including at page 21, line 24 ("Sf9 (*Sporodoptera frugiperda*)"); and page 21, line 25 ("Sf9 cells"). Thus, substitute Figures 1A, 1B and 2would not add new matter and their substitution into the specification is appropriate.

The amendments to the claims also do not add new matter. In particular, one of the amendments to claim 6 merely incorporates one of the diseases recited in claim 7 (IgE-mediated disease) into claim 6. The other amendment to claim 6, which recited that the antibody is free of significant agonistic activity, merely confirms the description of the antibody to what was deemed allowable in sister application, U.S. Serial No. 08/469,015, now U.S. Patent 6,004,552. Newly added claim 29, which recites that the antigen binding fragment is "selected from the group consisting of Fab, $F(ab)_2$ and Fv", is supported in the specification at page 7, line 14 ("fragments such as Fab, $F(ab)_2$, Fv and others which retain the antigen binding function of the antibody"). Newly added claim 30, which recites that the monoclonal antibody or the antigen binding fragment thereof is "humanized", is supported throughout the specification, including at page 7, lines 9 and 21-23 ("humanized antibodies").

For all these reasons, the amendments to the claims do not constitute new matter.

Respectfully submitted,

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Dated: September 18, 2001

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EXHIBIT A

6. A method for treating an IgE-mediated disease in a patient, the method comprising administering to a patient in need of such treatment a therapeutically effective amount of an anti-CD40 monoclonal antibody or an antigen binding fragment thereof, said monoclonal antibody or fragment thereof being free of significant agonistic activity and binding to a human CD40 antigen located on the surface of a human B cell, wherein the binding of the antibody to the CD40 antigen on the surface of said B cell prevents the growth or differentiation of the B cell.

8. The method of claim 6 wherein the monoclonal antibody is selected from the group consisting of 5D12, 3A8 and 3C6.

9. The method of claim 8 wherein the monoclonal antibody is 5D12.

10. The method of claim 8 wherein the monoclonal antibody is 3A8.

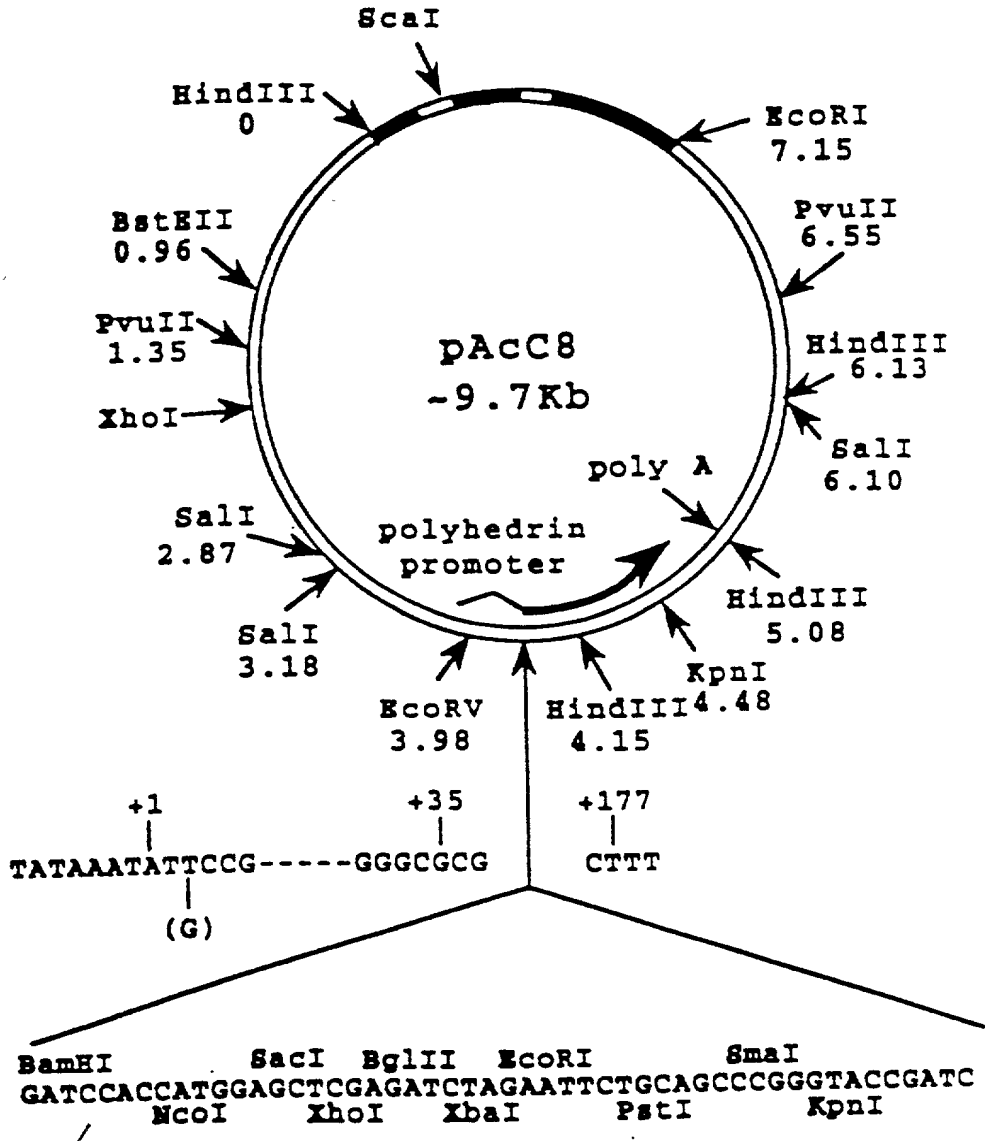
11. The method of claim 8 wherein the monoclonal antibody is 3C6.

29. The method of claim 6 wherein said antigen binding fragment of said monoclonal antibody is selected from the group consisting of Fab, $F(ab)_2$ and Fv.

30. The method of claim 6 wherein said monoclonal antibody or said antigen binding fragment thereof is humanized.

EXHIBIT B

6. (Amended) A method for [preventing or] treating an [antibody-mediated] IgE-mediated disease in a patient, the method comprising administering to a patient in need of such treatment a therapeutically effective amount of [a] an anti-CD40 monoclonal antibody or an antigen binding fragment thereof, said monoclonal antibody or fragment thereof being free of significant agonistic activity and binding [capable of binding] to a human CD40 antigen located on the surface of a human B cell, wherein the binding of the antibody to the CD40 antigen on the surface of said B cell prevents the growth or differentiation of the B cell[, in a pharmaceutically acceptable carrier].



SEQ ID NO: 1

Fig. 1A

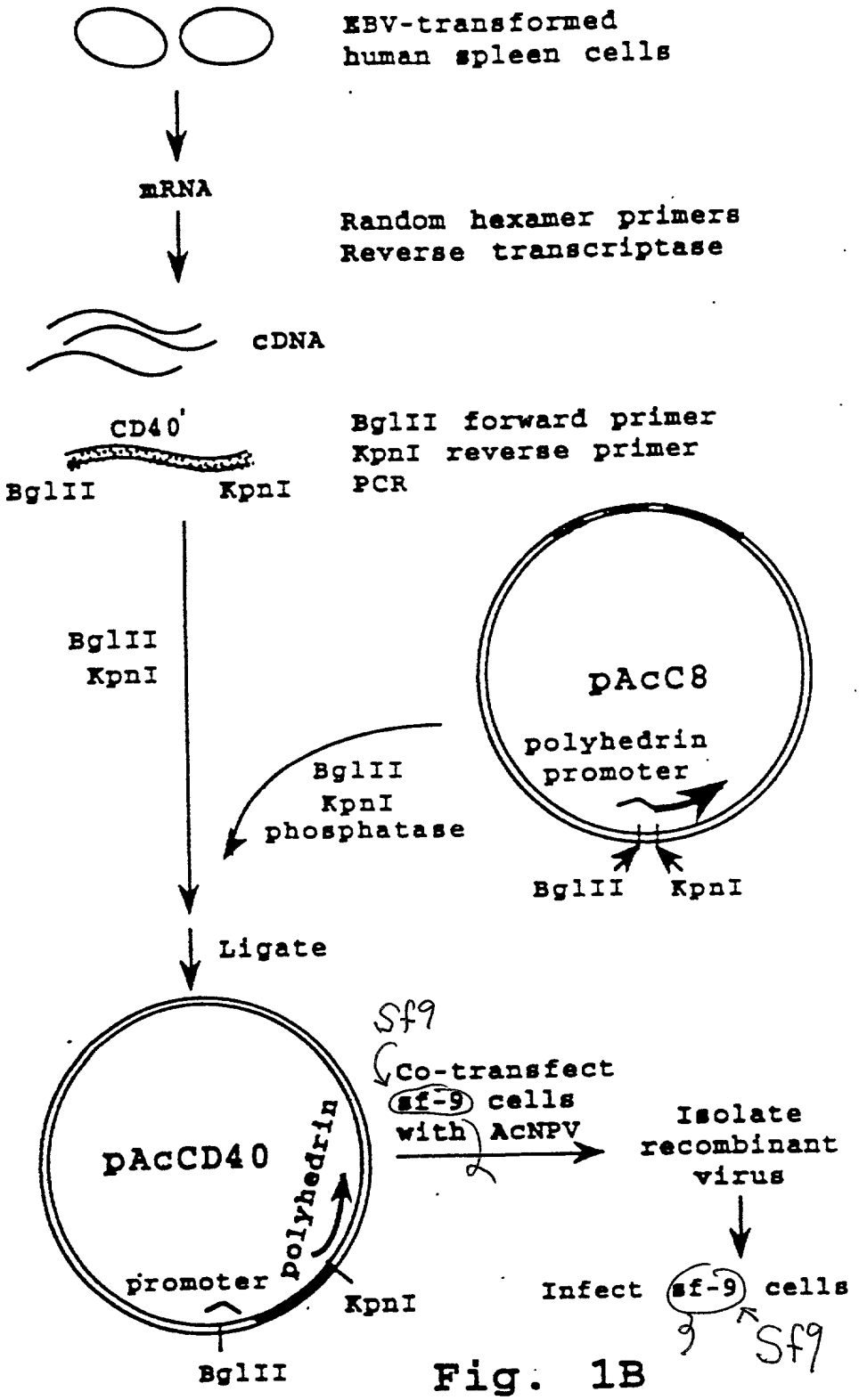

EBV-transformed
human spleen cells
mRNA
Random hexamer primers
Reverse transcriptase
cDNA
CD40
BglII
KpnI
BglII forward primer
KpnI reverse primer
PCR
BglII
KpnI
pAcC8
polyhedrin
promoter
BglII
KpnI
BglII
KpnI
phosphatase
Ligate
Sf9
Co-transfect
sf-9 cells
with AcNPV
Isolate
recombinant
virus
pAcCD40
polyhedrin
promoter
KpnI
BglII
Infect sf-9 cells
Sf9

Fig. 1B

Full length B7:

Forward MR67 5'-GCG CTGCAG CATCTGAAGCCATGGGCC-3' (307-324) (SEQ ID NO: 2)

Backward MR68 5'-CGC GGTACC TTGCTTCTGCGGACACTG-3' (1182-1199) (SEQ ID NO: 3)

Soluble B7:

Forward MR67 5'-GCG CTGCAG CATCTGAAGCCATGGGCC-3' (307-324) (SEQ ID NO: 2)

Backward MR145 5'-GCGC GGTACC <u>TTACTCCATGGGCATGTATTCCTCTTCCTC</u>GTTATCAGGAAAATGCTGTTG-3' (1022-1042) (SEQ ID NO: 4)

Full length CD40:

Forward MR108 5'-GCGT AGATCT GGTCTCACCTCGCCATGGTTCG-3' (34-55) (SEQ ID NO: 5)

Backward MR112 5'-GCGT GGTACC CCACACTCCTGGGTGGGTGCAGCC-3' (882-905) (SEQ ID NO: 6)

Soluble CD40:

Forward MR108 5'-GCGT AGATCT GGTCTCACCTCGCCATGGTTCG-3'. (34-55) (SEQ ID NO: 5)

Backward MR150 5'-GCGT GGTACC <u>TTACTCCATGGGCATGTATTCCTCTTCCTC</u>ATCAGTCTTGTTTGTGCCTGC-3' (575-596) (SEQ ID NO: 7)

Fig. 2